



Year: 2014

Safe, effective and durable epicardial left atrial appendage clip occlusion in patients with atrial fibrillation undergoing cardiac surgery: first long-term results from a prospective device trial

Emmert, Maximilian Y ; Puippe, Gilbert ; Baumüller, Stephan ; Alkadhi, Hatem ; Landmesser, Ulf ; Plass, Andre ; Bettex, Dominique ; Scherman, Jacques ; Grünenfelder, Jürg ; Genoni, Michele ; Falk, Volkmar ; Salzberg, Sacha P

Abstract: **OBJECTIVES:** Atrial fibrillation (AF) is a significant risk factor for embolic stroke originating from the left atrial appendage (LAA). This is the first report of long-term safety and efficacy data on LAA closure using a novel epicardial LAA clip device in patients undergoing cardiac surgery. **METHODS:** Forty patients with AF were enrolled in this prospective 'first-in-man' trial. The inclusion criterion was elective cardiac surgery in adult patients with AF for which a concomitant ablation procedure was planned. Intraoperative transoesophageal echocardiography (TEE) was used to exclude LAA thrombus at baseline and evaluate LAA perfusion after the procedure, while computed tomography (CT) was used for serial imagery workup at baseline, 3-, 12-, 24- and 36-month follow-up. **RESULTS:** Early mortality was 10% due to non-device-related reasons, and thus 36 patients were included in the follow-up consisting of 1285 patient-days and mean duration of 3.5 ± 0.5 years. On CT, clips were found to be stable, showing no secondary dislocation 36 months after surgery. No intracardial thrombi were seen, none of the LAA was reperfused and in regard to LAA stump, none of the patients demonstrated a residual neck >1 cm. Apart from one unrelated transient ischaemic attack (TIA) that occurred 2 years after surgery in a patient with carotid plaque, no other strokes and/or neurological events demonstrated in any of the studied patients during follow-up. **CONCLUSION:** This is the first prospective trial in which concomitant epicardial LAA occlusion using this novel epicardial LAA clip device is 100% effective, safe and durable in the long term. Closure of the LAA by epicardial clipping is applicable to all-comers regardless of LAA morphology. Minimal access epicardial LAA clip closure may become an interesting therapeutic option for patients in AF who are not amenable to anticoagulation and/or catheter closure. Further data are necessary to establish LAA occlusion as a true and viable therapy for stroke prevention. **CLINICAL TRIAL REGISTRATION:** The trial is registered at www.ClinicalTrials.gov, reference: NCT00567515.

DOI: <https://doi.org/10.1093/ejcts/ezt204>

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-78040>

Journal Article

Published Version

Originally published at:

Emmert, Maximilian Y; Puippe, Gilbert; Baumüller, Stephan; Alkadhi, Hatem; Landmesser, Ulf; Plass, Andre; Bettex, Dominique; Scherman, Jacques; Grünenfelder, Jürg; Genoni, Michele; Falk, Volkmar;

Salzberg, Sacha P (2014). Safe, effective and durable epicardial left atrial appendage clip occlusion in patients with atrial fibrillation undergoing cardiac surgery: first long-term results from a prospective device trial. *European Journal of Cardio-Thoracic Surgery*, 45(1):126-131.
DOI: <https://doi.org/10.1093/ejcts/ezt204>

Safe, effective and durable epicardial left atrial appendage clip occlusion in patients with atrial fibrillation undergoing cardiac surgery: first long-term results from a prospective device trial

Maximilian Y. Emmert^a, Gilbert Puippe^b, Stephan Baumüller^b, Hatem Alkadhi^b, Ulf Landmesser^c,
Andre Plass^a, Dominique Bettex^d, Jacques Scherman^a, Jürg Grünenfelder^a, Michele Genoni^e,
Volkmar Falk^a and Sacha P. Salzberg^{a,*}

^a Clinic for Cardiovascular Surgery, University Hospital Zurich, Zurich, Switzerland

^b Institute of Diagnostic and Interventional Radiology, University Hospital Zurich, Zurich, Switzerland

^c Clinic for Cardiology, University Hospital Zurich, Zurich, Switzerland

^d Institute for Anesthesiology, University Hospital Zurich, Zurich, Switzerland

^e Clinic for Cardiac Surgery, Triemli Hospital Zurich, Zurich, Switzerland

* Corresponding author. Clinic for Cardiovascular Surgery, University Hospital Zurich, Rämistrasse 100, CH - 8091 Zurich, Switzerland.
Tel: +41-44-2559362; fax: +41-44-2555047; e-mail: sach.salzberg@gmail.com (S.P. Salzberg).

Received 31 January 2013; received in revised form 13 March 2013; accepted 13 March 2013

Abstract

OBJECTIVES: Atrial fibrillation (AF) is a significant risk factor for embolic stroke originating from the left atrial appendage (LAA). This is the first report of long-term safety and efficacy data on LAA closure using a novel epicardial LAA clip device in patients undergoing cardiac surgery.

METHODS: Forty patients with AF were enrolled in this prospective 'first-in-man' trial. The inclusion criterion was elective cardiac surgery in adult patients with AF for which a concomitant ablation procedure was planned. Intraoperative transoesophageal echocardiography (TEE) was used to exclude LAA thrombus at baseline and evaluate LAA perfusion after the procedure, while computed tomography (CT) was used for serial imagery workup at baseline, 3-, 12-, 24- and 36-month follow-up.

RESULTS: Early mortality was 10% due to non-device-related reasons, and thus 36 patients were included in the follow-up consisting of 1285 patient-days and mean duration of 3.5 ± 0.5 years. On CT, clips were found to be stable, showing no secondary dislocation 36 months after surgery. No intracardial thrombi were seen, none of the LAA was reperused and in regard to LAA stump, none of the patients demonstrated a residual neck >1 cm. Apart from one unrelated transient ischaemic attack (TIA) that occurred 2 years after surgery in a patient with carotid plaque, no other strokes and/or neurological events demonstrated in any of the studied patients during follow-up.

CONCLUSION: This is the first prospective trial in which concomitant epicardial LAA occlusion using this novel epicardial LAA clip device is 100% effective, safe and durable in the long term. Closure of the LAA by epicardial clipping is applicable to all-comers regardless of LAA morphology. Minimal access epicardial LAA clip closure may become an interesting therapeutic option for patients in AF who are not amenable to anticoagulation and/or catheter closure. Further data are necessary to establish LAA occlusion as a true and viable therapy for stroke prevention.

CLINICAL TRIAL REGISTRATION: The trial is registered at www.ClinicalTrials.gov, reference: NCT00567515.

Keywords: Left atrial appendage • Stroke • TIA • Atrial fibrillation • Epicardial clip occlusion • Anticoagulation

INTRODUCTION

Atrial fibrillation (AF) is a well-established risk factor for the occurrence of stroke, and the thrombo-embolic origin in AF is very often related to the left atrial appendage (LAA) [1]. The standard of care for medical management of patients with AF remains oral anticoagulation [2, 3], and current guidelines recommend treatment of patients with a CHA₂DS₂-VASC >1 [2, 3].

In this regard, recent data indicate that LAA closure may be less inferior to anticoagulation in patients with AF in whom oral

anticoagulation was deemed unsuitable [4]. Just recently, the European Society of Cardiology (ESC) has recommended that if patients are not amenable to anticoagulation (elevated CHA₂DS₂-VASC and/or HAS-BLED scores), LAA occlusion may be warranted [2, 3]. Percutaneous approaches to LAA closure have set the basis for treating AF patients with contraindications to anticoagulation (elevated CHA₂DS₂-VASC and/or HAS-BLED scores). In published series, anatomy-based selection for closure devices is necessary to accommodate individual anatomical variations. These anatomical limitations do not apply to the epicardial

approach; however, current surgical closure offers only suboptimal results [5]. To the contrary, recent data indicate that the use of an epicardial LAA clip device during elective open heart surgery is safe and provides excellent early outcomes at 3 months after surgery [6, 7]. However, so far, only short-term reports are available for epicardial LAA clip occlusion while the long-term efficacy of this therapy concept remains to be elucidated.

In the present prospective 'first-in-man' clinical trial, for the first time, we report long-term outcomes of epicardial LAA clip occlusion in patients undergoing elective open heart surgery.

MATERIALS AND METHODS

This prospective device trial being registered at www.ClinicalTrials.gov (reference: NCT00567515), began in September 2007 with enrolment and was completed in July 2009 with a total of 40 patients with AF undergoing open heart surgery. While early outcome data for the initial 34 patients with regard to the feasibility of epicardial LAA clip placement and safety have been described previously [7], in the present study, and for the first time, we report long-term outcomes of epicardial LAA clip occlusion in patients undergoing elective open heart surgery.

The primary inclusion criterion was elective cardiac surgery in adult patients with AF for which an ablation procedure was planned. Exclusion criteria were reoperation, known thrombus in the LAA, patients from the intensive care unit, a history of pericarditis, recent myocardial infarction (<90 days) and a known allergy to the devices component (Supplementary Table 1). Computed tomography (CT) was used preoperatively to assess anatomy of the left atrium, pulmonary veins and LAA. Intraoperative transoesophageal echocardiography (TEE) was used to rule out LAA thrombus at baseline (exclusion criteria) and to evaluate LAA perfusion at the end of the procedure. Patients underwent serial follow-up after 3 months, and then yearly up to 3 years after surgery. Clinical follow-up comprised clinical status, laboratory examination; electrocardiogram, chest X-ray and CT workup [7]. After surgery, it was recommended to cease anticoagulation after 3 months. If in sinus rhythm, then aspirin 100 mg/day, and if in AF 300 mg/day was recommended.

Device description

The LAA Clip System (Atriclip, Atricure, Dayton, OH, USA) consists of a self-closing, implantable clip, a disposable selection guide is used to choose between the four available clip sizes (35,

40, 45 and 50 mm). When closed, the clip applies uniform pressure over the length of the two parallel branches to ensure consistent, reproducible and secure occlusion at the site of the basis of the LAA as demonstrated in the pre-clinical work [8]. For the initial trial, a reusable deployment tool was used. For market introduction, the deployment tool has since been redesigned and is a complete disposable set with the clip loaded within (Fig. 1).

Computed tomography protocol

All baseline and follow-up CT scans were performed according to the previously published protocol [7] using a dual-source CT scanner system with non-ionic contrast medium, standard scanning and image reconstruction parameters. In brief, LAA neck diameter was preoperatively measured on curved multiplanar reformations through the LAA. The LAA patency was visually analysed by two experienced independent readers in consensus. Patency was defined as the presence of contrast material within the entire LAA. Clip stability was assessed using two different measurements. In patients with contraindication to CT, such as impaired kidney function or refusal to undergo CT, serial chest radiography was deemed sufficient to assess the stability of implant. In all others, CT scan was used to precisely assess clip position and effect on surrounding structures.

This research was conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000, and all patients gave informed written consent.

Statistical analysis

The Kruskal-Wallis test was used to test for significant changes between the parameters average heart rate and heart rate variability during scanning, as well as between the clip location (i.e. distances and angles), LA diameters and LV function parameters across the CT examinations at different dates. A *P*-value of <0.05 was considered significant. Statistical analysis was performed using commercially available software (SPSS, release 15.0, Chicago, IL, USA).

RESULTS

Mortality and complications

At total of 40 patients were included in this prospective device trial. While early mortality was 10% (4 of 40 patients) due to non-device-related reasons comprising iatrogenic lung bleed (postoperative day 1), acute postoperative hepatic failure (postoperative day 16), bleeding due to aortic tear at aortotomy suture line (postoperative day 20) and out of hospital over anticoagulation-related tamponade (postoperative day 24) [7], a total of 36 patients (36 of 40, 90% of the initial cohort) could be successfully included in the follow-up assessments (Fig. 2).

In the follow-up cohort (*n* = 36, 100%), mean follow-up consisted of 1285 patient-days and mean duration of 3.5 ± 0.5 years. All 36 patients underwent follow-up at our institution and, during visits, electrocardiogram, laboratory workup and imaging

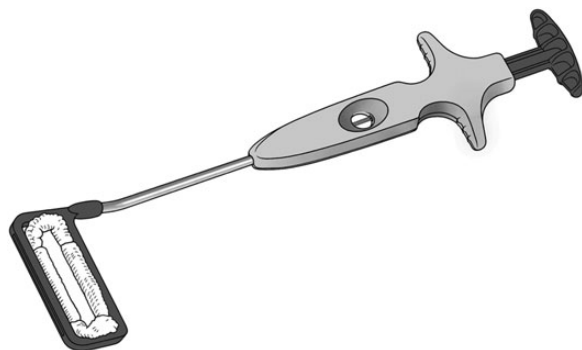


Figure 1: LAA clip occlusion device.

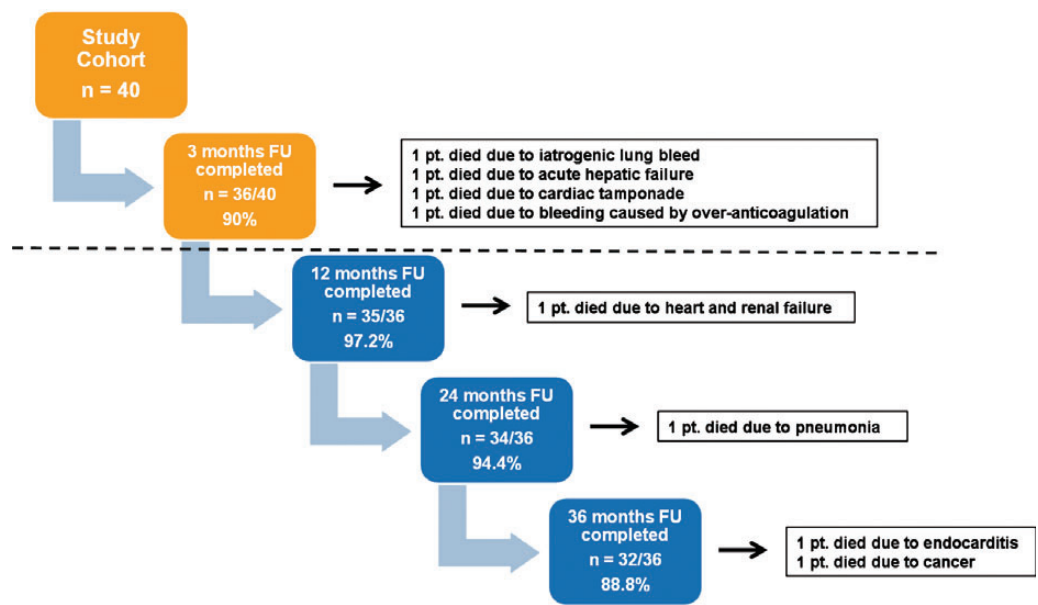


Figure 2: Study flow chart and follow-up. FU: follow-up.

examinations were performed. During the 3-year follow-up period, 4 patients (4 of 36; 11.1%) died due to non-device-related reasons including heart and renal failure ($n=1$, 8 months post-operatively), pneumonia ($n=1$, 22 months postoperatively), mitral valve endocarditis ($n=1$, 28 months postoperatively) and generalized cancer ($n=1$, 32 months postoperatively). Thus, 35 patients completed 1 year follow-up (35 of 36, 97.2%), 34 patients the 2-year follow-up (34 of 36, 94.4%) and 32 patients the 3-year follow-up (32 of 36, 88.8%). None of these deaths was related to the device or study participation, as demonstrated by an independent Autopsy report and Data Safety Monitoring Board review. The occurrence of cardiac and non-cardiac complications during follow-up is summarized in Table 1.

Occurrence of stroke and neurological events

Only one transient ischaemic attack (TIA) occurred in one patient 2 years after surgery (78-year old patient, $\text{CHA}_2\text{DS}_2\text{-VASC}=4$) in the setting of documented sinus rhythm with only aspirin and discontinued statins (Table 1). On CT and TEE, the LAA was occluded and no intracavitary thrombi were seen. This event was thought to be due to carotid plaque, statin treatment and anticoagulation were reinstituted, and no further ischaemic event occurred. In all other patients during follow-up, no strokes, TIA or neurological events occurred (0 of 36, 0.0%).

Heart rhythm and the need for anticoagulation

At 3 years, 22 patients were in sinus rhythm (22 of 32, 68.8%) and of the 10 in AF (10 of 32, 31.2%), only 3 (3 of 10, 30.0%) were still being anticoagulated with warfarin (Fig. 3). The mean $\text{CHA}_2\text{DS}_2\text{-VASC}$ Score of the entire study cohort ($n=40$) was 3.7 ± 1.7 points.

Imaging findings

On CT, LAA clips were found to be stable, showing no secondary dislocation (Table 2). Intracardial thrombi were not seen, and

Table 1: Mortality and major complications

Summary of mortality and adverse events	Number of patients (n = 36)
Overall mortality	4 (10.8%)
Device-related mortality	0 (0%)
Stroke	0 (0%)
Transient ischaemic attack	1 (2.7%)
Myocardial infarction	1 (2.7%)
Heart failure	1 (2.7%)
Arrhythmia	1 (2.7%)
Endocarditis	1 (2.7%)
Renal failure	1 (2.7%)
Pulmonary failure	0 (0%)
Liver failure	1 (2.7%)
Pneumonia	2 (5.2%)
Malignancy	1 (2.7%)

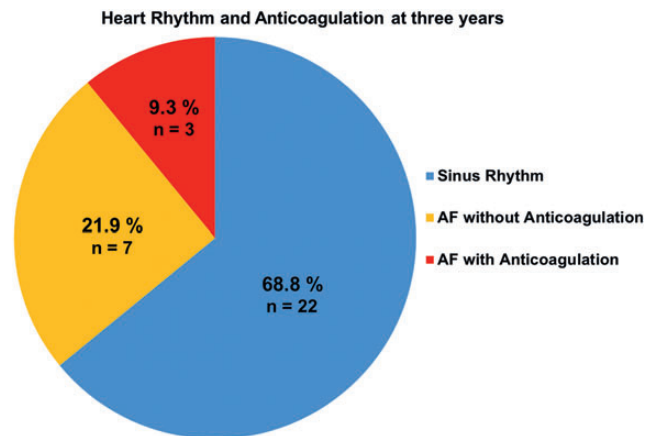


Figure 3: Heart rhythm and anticoagulation status 3 years after clip implantation. At 3 years following clip implantation, 22 patients were in sinus rhythm (22 of 32, 68.8%) and of the 10 patients being in atrial fibrillation, 7 patients did not require the continuation of anticoagulation treatment (7 of 32, 21.9%), while 3 patients (3 of 32, 9.3%) were still being anticoagulated with warfarin.

Table 2: Computed tomography findings at twelve-, twenty-four, and thirty-six month follow-up after LAA clip surgery

Follow		Postoperative	3 months	1 year	2 years	3 years	P-value ^a
Time interval ^b (days)	SD \pm mean	7 \pm 5	116 \pm 35	383 \pm 46	749 \pm 39	1101 \pm 17	
	Range	4–20	85–167	338–545	654–849	1078–1143	
Residual LAA perfusion		none	none	none	none	none	
First distance to CX (mm)	SD \pm mean	18 \pm 5	17 \pm 4	16 \pm 5	16 \pm 5	16 \pm 5	0.18
	Range	9–29	12–29	8–27	8–25	9–25	
Second distance to CX (mm)	SD \pm mean	32 \pm 8	34 \pm 8	34 \pm 8	32 \pm 7	33 \pm 7	0.81
	Range	20–49	12–29	23–46	21–45	21–43	
Angle (degree)	SD \pm mean	39 \pm 22	41 \pm 16	37 \pm 17	39 \pm 19	40 \pm 21	0.11
	Range	11–96	12–70	9–66	9–80	11–81	
LAA stump > 1cm		none	none	none	none	none	

^aFriedman's 2-way paired ANOVA. The level of significance is 0.05.

^bTime Interval displayed as time between surgery and follow up.

LAA: left atrial appendage; CX: circumflex artery.

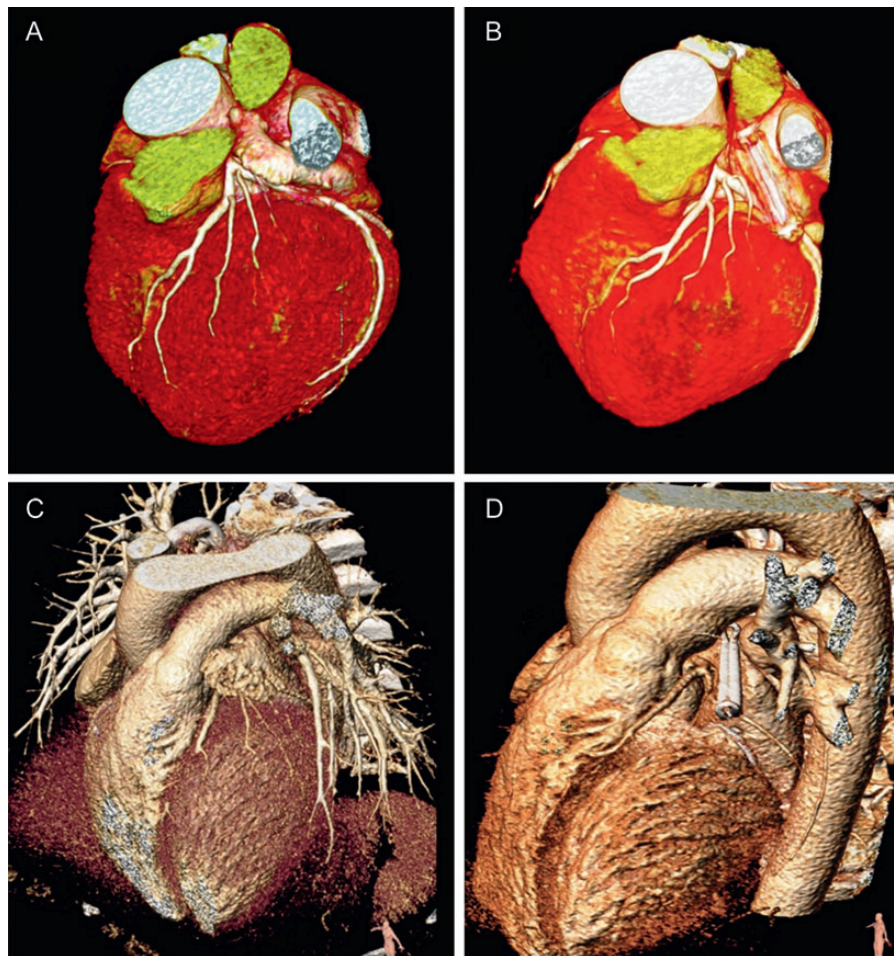


Figure 4: Computed tomography (CT) before and at 3-year follow-up after clip implantation. Exemplary CT before clip placement (A and C) and after clip implantation depicting the clip in stable position and fully excluding the left atrial appendage at a 3-year follow-up (B and D).

none of the LAAs were reperfused. LAA occlusion was total and complete in all patients (32 of 32, 100%) (Figs 4 and 5). In regard to LAA stump, none of the patients demonstrated a residual neck of >1 cm. Importantly, the results of imaging follow-up were consistent after 3 years follow-up in all patients. On chest radiography, the stability of the implant was also clearly documented.

DISCUSSION

Herein we report the first long-term outcome data on epicardial LAA clip application during open heart surgery. In addition to being 100% effective and safe in the short term [6, 7, 8], the results of this prospective device trial demonstrate the durable

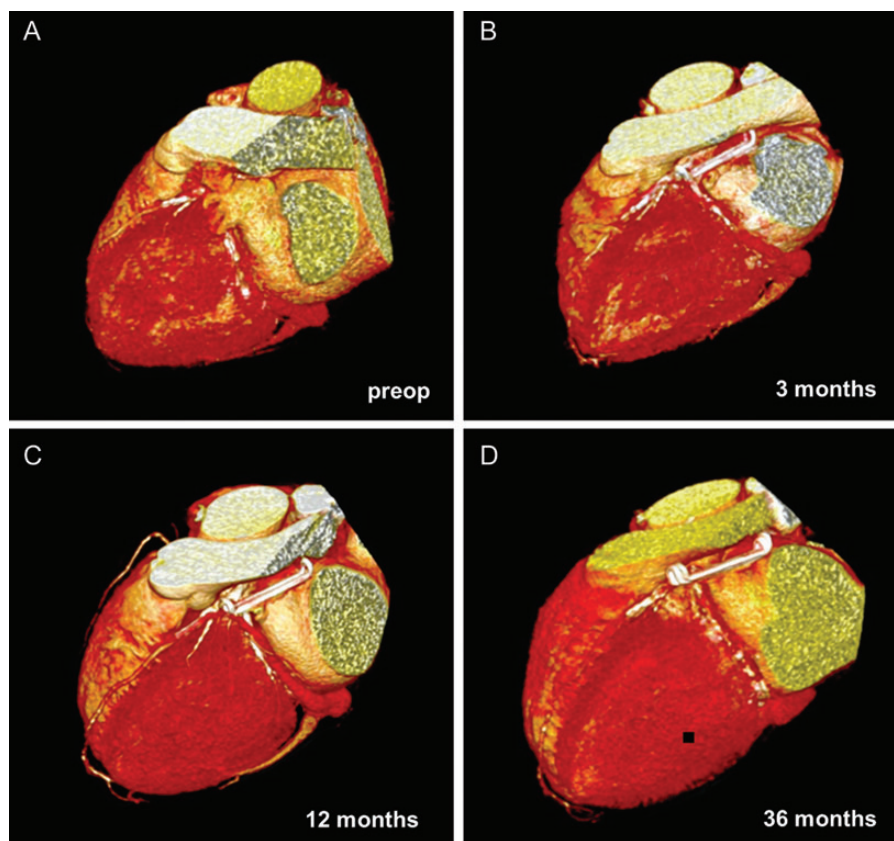


Figure 5: *In vivo* monitoring of clip safety and stability using serial computed tomography (CT). CT image series of an exemplary patient before (A), at 3 months (B), 12 months (C) and at 36 months (D) after implantation indicating a stable clip position and durable left atrial appendage occlusion early postoperatively as well as throughout the entire follow-up period.

occlusion of the LAA for over 3 years with excellent clinical outcomes. Importantly, during follow-up, no strokes occurred and anticoagulation could be often discontinued, most often decided by general practitioners and referring cardiologists. Moreover, our data indicate that successful closure of the LAA by epicardial clipping is applicable regardless of LAA morphology. Overall, no device-related complications occurred, the device performed as it was designed to and fulfilled its purpose of totally excluding the LAA from circulation.

LAA occlusion is performed to decrease the incidence of stroke and anticoagulation-related bleeding, and it appears that these complications did not occur in our series. When compared with the CHA₂DS-VASC score, we have seen a very low rate of thrombo-embolic complications in our series. Considering a mean CHA₂DS-VASC score of close to 4, the expected stroke rate would have been well above 10% [9].

It is obvious that the underlying cause of stroke in this population is multifactorial, and not only related to the LAA [10]. That is why we believe that sufficient anti platelet aggregation and also statin treatment, when indicated, must be instituted in these patients when not in sinus rhythm. However, it is important to note that the CHA₂DS-VASC Score does not take into account LAA perfusion. This score was created on patients in AF with LAA. Therefore, we believe that it is time for it to be revised, or at least used with precaution, as patients with occluded LAAs will present with a decreased risk profile in the setting of non-valvular AF. With this in mind, it appears that despite lack of data, closure of the LAA has become a well-accepted therapeutic option for patients not amenable for anticoagulation with AF.

Only one large trial allows the conclusion that effective LAA closure provides stroke prevention [4], even though closure was far from complete in this series. For precisely this purpose we have initiated the creation of a web-based registry (www.laacr.org) to collect long-term follow-up data on all patients undergoing a surgical LAA closure.

While there are several methods to close the LAA, it is obvious that the limitation of surgical LAA occlusion is the invasiveness of the procedure, however effective it might be. For patients undergoing heart surgery, it is our belief that LAA resection or clipping should therefore be performed in the setting of AF or even without AF, but with significant risk factors. This is not only meant for long-term protection but also in regard to the peri-operative risk of thrombo-embolic complications [11]. Only effective LAA therapies providing complete and durable occlusion should be used, as incomplete occlusion will worsen the risk profile and subject these patients to increased risk [5]. In their recent study, Kanderian *et al.* [5] assessed 137 patients who underwent surgical closure and demonstrated that there is a high occurrence of unsuccessful surgical LAA closure. On the other hand, the results for thoracoscopic ablations for stand-alone surgical treatment of AF, in which the LAA is removed by stapling, are excellent [12]. Thus, whatever option is chosen to address the LAA, documented complete LAA occlusion is essential [5, 7] and must be achieved.

In addition, also endocardial approaches to closing the LAA are currently being used. As surgeons, we believe that the high anatomical variability [13] may make a more tailored approach necessary. Currently, very scarce data are available on these new approaches; nevertheless, the Protect AF trial [4] set the path for

this new therapeutic option. Currently, and when compared with our study, in none of the published series a 100% effectiveness is reported for immediate LAA occlusion, and this is a major concern as these patients with contraindications to oral anticoagulation will then require just this [14, 15].

Another argument in favour of surgical closure is the electrophysiological role the LAA plays, and in particular in AF recurrences after left-sided catheter ablation for AF [16], in regard to this specific issue, we have demonstrated complete electrical isolation after LAA clip placement [17]. Therefore, it appears that the epicardial approach of LAA removal by staplers or LAA clipping may also provide adjunctive electrophysiological benefits.

Limitations

This was a surgical trial designed to evaluate this new device as a concomitant therapy option in patients undergoing cardiac surgery. The real potential for impact comes in the setting of the treatment for lone AF even in a stroke-prevention scenario, where stand-alone LAA therapies might effectively impact medicine.

CONCLUSION

This prospective device trial demonstrates, for the first time, the long-term safety, durability and efficacy of epicardial LAA clip occlusion using a novel epicardial clip device during cardiac surgery. In this series, no strokes occurred during follow-up, and anticoagulation could often be discontinued. The results show that successful epicardial LAA clip occlusion is applicable to all-comers regardless of LAA morphology. Minimally invasive epicardial LAA clip closure may represent an interesting therapeutic strategy for patients in AF who are not amenable to anticoagulation. Further studies are necessary to establish LAA occlusion as a true and viable therapy strategy for stroke prevention.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

Funding

This research was funded by an unrestricted research grant from Atricure.

Conflict of interest: Sacha P. Salzberg is a consultant for Atricure and has received speaker fees.

REFERENCES

- [1] Frost L, Engholm G, Johnsen S, Moller H, Husted S. Incident stroke after discharge from the hospital with a diagnosis of atrial fibrillation. *Am J Med* 2000;108:36–40.
- [2] Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S *et al.* Guidelines for the management of atrial fibrillation: the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC). *Eur Heart J* 2010;31:2369–429.
- [3] Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S *et al.* Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Europace* 2010;12:1360–420.
- [4] Holmes DR, Reddy VY, Turi ZG, Doshi SK, Sievert H, Buchbinder M *et al.* Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. *Lancet* 2009;374:534–42.
- [5] Kanderian AS, Gillinov AM, Pettersson GB, Blackstone E, Klein AL. Success of surgical left atrial appendage closure: assessment by transesophageal echocardiography. *J Am Coll Cardiol* 2008;52:924–9.
- [6] Ailawadi G, Gerdtsch MW, Harvey RL, Hooker RL, Damiano RJ Jr, Salamon T *et al.* Exclusion of the left atrial appendage with a novel device: early results of a multicenter trial. *J Thorac Cardiovasc Surg* 2011;142:1002–9, 1009 e1001.
- [7] Salzberg SP, Plass A, Emmert MY, Desbiolles L, Alkadhi H, Grunfelder J *et al.* Left atrial appendage clip occlusion: early clinical results. *J Thorac Cardiovasc Surg* 2010;139:1269–74.
- [8] Salzberg SP, Gillinov AM, Anyanwu A, Castillo J, Filsoufi F, Adams DH. Surgical left atrial appendage occlusion: evaluation of a novel device with magnetic resonance imaging. *Eur J Cardiothorac Surg* 2008;34:766–70.
- [9] Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the national registry of atrial fibrillation. *JAMA* 2001;285:2864–70.
- [10] Tugcu A, Okajima K, Jin Z, Rundek T, Homma S, Sacco RL *et al.* Septal pouch in the left atrium and risk of ischemic stroke. *JACC Cardiovasc Imaging* 2010;3:1276–83.
- [11] Ryan K, Norbert B, John C. Perioperative Management Routine left atrial appendage ligation during cardiac surgery may prevent postoperative atrial fibrillation-related cerebrovascular accident. *J Thorac Cardiovasc Surg* 2013;145:582–9.
- [12] Krul SP, Driessen AH, Zwinderman AH, van Boven WJ, Wilde AA, de Bakker JM *et al.* Navigating the mini-maze: systematic review of the first results and progress of minimally-invasive surgery in the treatment of atrial fibrillation. *Int J Cardiol* 2013;166:132–40.
- [13] Di Biase L, Santangeli P, Anselmino M, Mohanty P, Salvetti I, Gili S *et al.* Does the left atrial appendage morphology correlate with the risk of stroke in patients with atrial fibrillation? Results from a multicenter study. *J Am Coll Cardiol* 2012;60:531–8.
- [14] Shetty R, Leitner JP, Zhang M. Percutaneous catheter-based left atrial appendage ligation and management of periprocedural left atrial appendage perforation with the lariat suture delivery system. *J Invasive Cardiol* 2012;24:E289–93.
- [15] Bartus K, Han FT, Bednarek J, Myc J, Kapelak B, Sadowski J *et al.* Percutaneous left atrial appendage suture ligation using the lariat device in patients with atrial fibrillation: initial clinical experience. *J Am Coll Cardiol* 2012; pii:S07351097(12)03035-5.
- [16] Di Biase L, Burkhardt JD, Mohanty P, Sanchez J, Mohanty S, Horton R *et al.* Left atrial appendage: an underrecognized trigger site of atrial fibrillation. *Circulation* 2010;122:109–18.
- [17] Starck CT, Steffel J, Emmert MY, Plass A, Mahapatra S, Falk V *et al.* Epicardial left atrial appendage clip occlusion also provides the electrical isolation of the left atrial appendage. *Interact CardioVasc Thorac Surg* 2012;15:416–8.